

OPTICAL DETECTOR SYSTEM

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims benefit of prior co-pending Provisional Application 60/400,884, filed, 08/02/2002, and entitled A Modular Device for Microscale Biotoxin Detection.

STATEMENT OF GOVERNMENT INTEREST

[0002] This invention was made with Government support under contract no. DE - AC04 - 94AL85000 awarded by the U. S. Department of Energy to Sandia Corporation. The Government has certain rights in the invention.

FIELD OF THE INVENTION

[0003] The invention is directed to a modular optical detector system that can be used in combination with capillary chromatographic and microchip-based chemical analysis systems. The presence of molecules or molecular species in liquid mixtures in sub-nanomolar concentrations is determined by inducing fluorescence with exciting radiation and detecting the emitted fluorescence.

BACKGROUND OF THE INVENTION

[0004] Recent advances in miniaturization, and particularly in the field of microelectro-mechanical structures (MEMS), have led to the development of microfluidic devices that are designed, in part, to perform a multitude of chemical and physical processes on a micro-scale. The attraction of these microsystems lies in the fact that miniaturization provides for substantial advantages in terms of cost, speed, the capability for easy automation,

reproducibility, rapidity of analysis, and the need for only very small (μL) samples. As a consequence, microsystems in the form of microfluidic devices are becoming increasingly important in such diverse fields as DNA sequencing, immunochromatography, analysis and identification of explosives, chemical and biological warfare agents, and synthesis of chemicals and drugs.

[0005] Because only minute amounts of sample are required these microchemical analysis systems are particularly attractive for not only for rapid chemical analysis but also for the ability to analyze accurately a large number of samples in a short period of time. However, there remain problems in reproducibly detecting and measuring low concentrations of chemicals conveniently, safely and quickly.

[0006] Laser-induced fluorescence is one of the more sensitive detection methods available, being responsive to picomolar concentrations of analytes and thus, is ideally suited to the small volumes employed in capillary or microchip-based chemical analysis systems.

SUMMARY OF THE INVENTION

[0007] Accordingly, an object of this invention is to provide a modular optical detector system for detecting the presence of molecules or molecular species by inducing fluorescence with exciting radiation and detecting the emitted fluorescence. Because the invention is capable of accurately detecting and measuring picomolar concentrations it is designed for use with microchemical analysis systems generally and capillary chromatographic systems in particular.

[0008] A further object of the invention is to provide a modular system,

wherein modularity is the ability to replace various elements, including optical elements, of the detector system without requiring extensive realignment or recalibration of the components. The modular concept provides for the use of a wide variety of components to fit particular needs. For example, almost any light source that can cause molecules to fluoresce, either naturally or tagged with a fluorophore, can be used in this system. Potential light sources that can be used in the optical detector system can include those that emit light from the infrared to the ultraviolet. These include, but are not limited to light-emitting diodes, laser diodes, vertical cavity surface emitting lasers (VCSELs), vertical external cavity surface emitting lasers (VECSELs), dipole pumped solid state (DPSS) lasers or fiber optic connections that are subsequently coupled to light sources such as large laser systems, laser diodes or lamps. Optical elements can include lenses and filters either singly or in combination, that are totally interchangeable to accommodate the light source. Filters can be put in place to filter out background radiation. More complex optical elements such as blazed or holographic gratings can be included to condition the excitation and emission radiation in ways that cannot be accomplished by filters alone.

[0009] Potential detection means for this optical system can include photomultiplier tubes, photodiodes, avalanche photodiodes or array detectors such as photodiode arrays and charge-coupled devices, or photosensitive detectors. These detection means can be run in analog signal collection mode, phase locked, or photon counting mode.

[0010] A design feature of the optical detector system is reduced user interaction with the system. By limiting the user interaction to a single

mechanical optical adjustment, the time required for aligning the system to a detection region, wherein the detection region can be a portion of a separation channel, is reduced and the potential for user-caused system misalignment is minimized. Once the entire system is initially aligned during assembly, the user need only adjust the lateral position of a beam positioning block using a translation screw for subsequent alignments to the separation channel.

[0011] In one embodiment, the invention is directed to an optical detector system that includes:

A light source for generating an exciting light beam;
optical elements for collimating and directing the exciting light beam onto a sample in a detection region and collecting radiation emitted from the detection region; and
detection means for receiving the emitted radiation.

[0012] In another embodiment, the light source is a laser, the detection means is a photomultiplier tube and said optical elements, further including a beam steering mirror configuration, are used in conjunction with the laser light source.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] Figure 1 is a view of an embodiment of the invention showing an exterior view (Fig. 1a) and with the cover removed (Fig. 1b).

[0014] Figure 2 is an epi-fluorescence configuration of the invention.

[0015] Figure 3 shows a second configuration for delivering a focused beam of radiation.

[0016] Figure 4 shows a dovetail rail assembly for holding the excitation

source.

DETAILED DESCRIPTION OF THE INVENTION

[0017] Referring now to the drawings, FIG. 1a shows an exterior view of the optical detector system, indicated generally at **100**. The optical detector system is comprised generally of two modules, optics module (**B**) that contains the light source and associated optical elements for generating, collimating, shaping the light beam, directing the resulting light beam onto a detection region, and collecting the resulting fluorescent radiation. Detector module (**C**) contains detection means for receiving and analyzing the emitted radiation. Module **B** is in optical communication with module **C** and, as illustrated in FIG. 1a can be superposed onto module **C**. The two-tier modular design illustrated in FIG. 1a, wherein the light source and associated optical means are combined with detection means in a unitary structure provides for isolating stray light arising from the excitation source from the detector. Moreover, the totally enclosed package excludes room light. The terms "light" and "radiation" will be used herein interchangeably and synonymously.

[0018] FIG. 1b is a view of the detector system with detector cover **125** removed showing the general arrangement and features of the optics system including excitation source **110**, a beam steering mirror system **112**, and optical means **245** for focusing exciting radiation onto a sample and for collecting the emitted radiation.

[0019] It will be appreciated by those of skill in the optics art, that for analysis purposes is advantageous to employ light that is of the highest quality. Therefore, it is desirable to provide means for proper conditioning of the light beam. FIG. 1b also shows one aspect of the detector system in

which beam steering mirror system **112**, here comprising four beam steering mirrors, is part of an optical train used, in conjunction with a UV laser light source, to direct light to a detection area, through objective lens **245**. The novel folded path provided by this mirror configuration provides an optical path (4.5 to 5 inches) that is long enough so that a light beam can be conditioned properly, both spatially and spectrally within a confined space. For higher quality light sources the beam path can be shortened correspondingly. This steering mirror configuration can provide other advantages such as simplifying alignment of the light beam.

[0020] FIGs. 2 and 3 are cross-sectional views that illustrate the basic layout of the optical platform for two separate embodiments of the optical detector system. FIG. 2 shows a detector system, in an epi-fluorescence configuration and FIG. 3 shows an off-axis excitation configuration. Both configurations are arranged on a platform that is approximately 3.25 inches long, 2.25 inches wide and 1.3 inches tall.

[0021] Referring now to FIG. 2. In this configuration, the detector uses an epi-fluorescence optical configuration to deliver a focused beam of laser light to detection region **210** to excite sample molecules, thereby generating fluorescent radiation. The optics module **B** of optical detector system **100** contains a light source **220** that can be a generic light source. Potential light sources that could be coupled into this optical detector system are light-emitting diodes, laser diodes, VCSELs, VECSELs, DPSS lasers or fiber optic connections that can be subsequently coupled to light sources such as large laser systems, laser diodes or lamps. In the embodiment shown in FIG. 2 the light source is a laser and preferably a laser capable of generating light

having a wavelength of about 405 nm. As discussed above, the collimated beam can be reflected off dichroic reflectors or mirrors **112**, to reject some broadband emissions, before being steered onto optical means **240** and **245** contained in beam positioning block **235**. Additional excitation filters **275** can be positioned before beam positioning block **235** for increased spectral conditioning. The collimated beam is reflected off a dichroic filter **240** and finally focused onto the detection region **210** that can be the detection region of an associated microfluidic chip or chromatographic column with aspherical lens **245**. This same lens is used to collect fluorescence generated by the constituents of the sample in detection region **210**. The collimated radiation emitted by the sample is passed through dichroic filter **240** and into detector module **C** of optical detector system **100** where it can be directed onto radiation detection means, such as a photodetector. In the embodiment illustrated in FIG. 2, the emitted radiation is turned 90 degrees by reflection element **250** into a photodetector **255** that can be a photomultiplier tube. Before passing into the photodetector the collimated beam can be shaped and modified by being passed through filters and optical elements **260**. Light from light source **220** can be aligned to the detection area of a microchip or chromatographic column by translating beam steering block **235**, and optical means contained therein, back and forth across detection area **210** using translation screw **265**. The use of epi-fluorescence provides an additional advantage in that there are no size constraints and thus high numeric aperture (NA) aspheric or ball-type lenses can be used as a collection optic. In one aspect of the invention, a 0.60 NA aspheric lens was used as the collection optic.

[0022] In a second embodiment (FIG. 3), a focused beam of light is delivered onto the detection region **210** at Brewster's angle for fused silica and the radiation emitted therefrom is collected and analyzed. Excitation light from light source **220**, is collimated by aspherical lens **225**. As in the embodiment above, the light source can be a generic light source. As before, light sources that could be coupled into this optical detector system are light-emitting diodes, laser diodes, VCSELs, VECSELs, DPSS lasers or fiber optic connections that can be subsequently coupled to light sources such as large laser systems, laser diodes or lamps. Here, as above, a laser having a wavelength of about 405 nm is used as a source of exciting radiation. To reject broadband emissions from light source **220**, excitation filters **275** can be positioned between the light source and beam steering mirror **310** to spectrally modify the collimated light beam. Turning mirror **310**, attached to an arm or beam positioning block **235**, is used to direct the beam upward to intersect detection region **210** directly above and centered on objective lens **245**. Transition screw **265** is used to translate beam steering block **235**, containing lens **245** and mirror **310**, laterally so the focused light beam and lens are positioned properly with respect to detection region **210**. In order to ensure that the light beam is intersecting the detection region, a fluorescent dye can be injected into the detection region to visualize the location of the beam. Lens **245** is used to collect the fluorescent radiation emitted from the detection region. As in the embodiment above, the collected fluorescent radiation is directed to the detector module (module **C**) of the optical detector system where the collected light passes through filters and lenses **260** to remove scattered and off-wavelength radiation and into a

radiation detection means such as photomultiplier tube **255**.

[0023] In keeping with an object of the invention, the ability to replace components without the necessity of realignment or recalibration, FIG. 4, shows a dovetail-aligned rail assembly, indicated generally at **400**. This assembly is a unitary structure that holds an excitation source, wherein said excitation source comprises light source **220** and associated collimating optics **225** and filters **275** in a stable, fixed relationship with one another and wherein the excitation source is demountably engaged on dovetail rail **415**. Not only does this unique feature provide for easy replacement of the light source and/or optics but also ensures that established alignment will be maintained if the rail assembly or any of its components are replaced.

[0024] A design feature of the optical detector system is reduced user interaction with the system. In this regard, optics module **B** incorporates a beam positioning block **235**, wherein said beam positioning block includes, at least, dichroic filter **240** and focusing/collection optic **245**. By limiting the user interaction to a single mechanical adjustment, the time required for aligning the system to a detection area is reduced and the potential for user-caused system failure is eliminated. Once the entire system is initially aligned, the user need only adjust the lateral position of beam positioning block **235** using translation screw **265** for subsequent alignments to a detection area. Alignment pins **115** are incorporated into the detector lid to reduce the magnitude of the adjustment made to translation screw **265** to achieve proper alignment.

[0025] It is contemplated that the novel modular optical detector system disclosed herein could be used in conjunction with a microfluidic chemical

analysis system and in particular with capillary chromatography systems.